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Original Article

Elranatamab in Heavily Pretreated Triple-class Refractory Multiple Myeloma: A Single-center Experience

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ABSTRACT

Aim: This study aimed to assess the real-world performance of elranatamab in terms of its effectiveness, safety, and tolerability among patients diagnosed with triple-class refractory-multiple myeloma (TCR-MM) who have undergone extensive prior treatment.

Methods: A retrospective review was conducted at a single medical center, involving 12 TCR-MM patients who received elranatamab. Data were analyzed on demographics, cytogenetics, disease burden, prior therapies, infectious complications, and survival outcomes. Responses were assessed according to International Myeloma Working Group criteria, and adverse events were graded per common terminology criteria for adverse events version 5.0.

Results: The overall response rate was 83.3%, with a median progression-free survival of 8.0 months and a median overall survival of 11.0 months. Common adverse events included grade ≥3 infections (75%) and cytokine release syndrome (CRS), which occurred in 41.7% of the participants, with only grade 1-2 CRS observed. No immune effector cell-associated neurotoxicity syndrome was reported.

Conclusion: Elranatamab demonstrated promising clinical efficacy and an acceptable safety profile in a heavily pretreated TCR-MM population. The elevated risk of infections necessitates close clinical surveillance.

Keywords: Multiple myeloma, antibodies, bispecific, cytokine release syndrome, immunotherapy, B-cell maturation antigen

Introduction

Multiple myeloma (MM) is a malignancy of plasma cells characterized by cycles of remission and relapse, eventually resistance to therapy. The advent of proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and monoclonal antibodies, particularly anti-cluster of differentiation (CD) 38 agents, has significantly extended survival in MM [1]. A subset of patients eventually becomes triple-class refractory (resistant to a PI, an IMiD, and an anti-CD38 monoclonal antibody), facing poor prognoses with a median overall survival (OS) frequently falling below one year [1]. Elranatamab, a humanised bispecific antibody designed to engage B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T-cells, enables T-cell-mediated cytotoxicity in a manner independent of major histocompatibility complex presentation [2]. Initial data from the MagnetisMM trials have shown encouraging clinical activity, with the MagnetisMM-3 study reporting an overall response rate (ORR) of 61% in the heavily pretreated subgroup [2]. Notably, elranatamab is administered subcutaneously, which reduces the severity of cytokine release syndrome (CRS) compared to intravenous BCMA therapies. Real-world data regarding the effectiveness, tolerability, and logistical considerations of elranatamab remain scarce. These insights are particularly important for institutions managing patients with multiple comorbidities, cumulative toxicities, and treatment fatigue-features common in the triple-refractory population. This paper presents a single-center experience evaluating elranatamab, in such a cohort, aiming to contextualize its clinical utility and safety profile outside of a controlled trial setting.

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Methods

Study Objective

The primary endpoint of this single-center retrospective study is to evaluate the ORR, progression-free survival (PFS), and OS in patients with heavily pretreated, triple-class refractory MM, treated with elranatamab. These outcomes are benchmarked against results from prospective clinical trials and published real-world evidence. The secondary end point is to assess the safety and tolerability of elranatamab in this population, with a specific focus on infectious complications and immune-related adverse events, including CRS and immune effector cell-associated neurotoxicity syndrome (ICANS).

Informed consent was obtained from all the patients for the use of medical data. Patient confidentiality was maintained throughout the study, in accordance with the Declaration of Helsinki. Approval was obtained from the Acıbadem University Ethics Committee for the study (decision no: 2025-08/64, date: 22.05.2025).

Study Design and Patient Selection

The study reviewed clinical records of 12 patients with confirmed TCR-MM who received elranatamab between 2023 and 2024. Inclusion required patients to be 18 years or older, have been documented as refractory to a PI, an IMiD, and an anti-CD38 monoclonal antibody, and to have received elranatamab via compassionate use, early access, or routine post-approval care.

Data Collection

Demographic, clinical, and laboratory data were extracted from electronic health records using a structured data abstraction form. Collected variables included age, gender, eastern cooperative oncology group performance status, number of prior lines of therapy, disease burden, presence of extramedullary disease, infection history, and baseline immune status defined by immunoglobulin G levels and cytomegalovirus (CMV) reactivation on follow-up. Cytogenetic risk profile was determined using the fluorescence *in situ* hybridization method by assessment of IGH/FGFR3, IGH/CCND1, IGH/CCND3, IGH/MAF, IGH/MAFB, IGH, 13q14 RB1, del D104S319, trisomy 12, 17p13.1 p53, CKS1B/CDKN2C, and MYC mutations. Elranatamab was administered subcutaneously at 12 mg on day 1.32 mg on day 4, and 72 mg on day 8, followed by weekly doses of 72 mg for six weeks, and then administration of 72 mg every two weeks until progression or adverse effects occurred. Premedication with 20 mg dexamethasone, paracetamol, diphenhydramine, and montelukast was given before every dose of elranatamab. All patients were admitted to the hospital for the first 5 days of elranatamab treatment to facilitate close monitoring of potential CRS.

The response evaluations at each clinical follow-up were done according to the International Myeloma Working Group (IMWG) criteria. Adverse events were graded per CTCAE v5.0 guidelines. The dates of disease progression or death for each patient were recorded and used for the survival analyses. A summary of baseline demographics and disease characteristics is presented in Table 1.

Outcome Measures

Responses were classified using IMWG guidelines. Adverse events were documented per CTCAE v5.0 criteria**.** CRS is a condition that occurs when the immune system reacts excessively, releasing cytokines. According to the American Society of Transplantation and Cellular Therapy consensus, CRS severity ranges from fever (grade 1) to life-threatening consequences (grade 4) [3].

Statistical Analysis

Kaplan-Meier analysis was employed for survival estimates. Statistical computations were performed using Statistical Package for the Social Sciences (SPSS) version 26 (SPSS Inc., Chicago, Ill., USA) and R version 4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

This retrospective analysis included 12 patients with triple-class refractory MM. All patients were refractory to at least one PI, one IMiD, and one anti-CD38 monoclonal antibody. The median number of prior lines of therapy was 6, reflecting a heavily pretreated population. At a median follow-up of 13 months, the ORR-defined as the proportion of patients achieving a very good partial response (VGPR), partial response (PR), or complete response (CR)-was 83.3%. This included 5 CR, (41.6%), 1 PR, (8.3%), and 4 VGPR (33.3%). Only two patients (16.6%) had stable or progressive disease as best response. The median PFS was 8.0 months, and the median OS was 11.0 months (Figures 1, 2). At the time of analysis, 9 of the 12 patients (75%) were still alive. The median number of elranatamab treatment cycles administered was 7. Most patients continued treatment beyond initial responses, with a few receiving more than 15 cycles.

Grade 3 or higher infections occurred in 75% of patients. CMV reactivation was documented in 25% of cases, indicating a need for routine virological surveillance. CRS occurred in 5 patients, 41.6% (grade 1 in 4 patients, 33.3%, and grade 2 in 1 patient, 8.3%). Only one patient needed tocilizumab treatment for CRS. ICANS was not reported in any patient. Grade 3 cytopenia was observed in 66.7% of the cohort, with 72.3% of patients requiring granulocyte colony-stimulating factor administration and 42.6% requiring platelet transfusions. Infections, CMV reactivation, and severe cytopenias were predominant causes for dose interruptions and reductions which were required in 75% of the patients.

Discussion

The introduction of BCMA-targeted bispecific antibodies has significantly expanded the therapeutic armamentarium for patients with TCR-MM. Elranatamab, a subcutaneously administered bispecific antibody engaging CD3+ T-cells and BCMA+ myeloma cells, has emerged as a promising agent. This study represents a single-center real-world analysis that reinforces the clinical benefit observed in pivotal trials while offering insights into treatment logistics, adverse event profiles, and infection risks in a real-world population.

In our cohort of 12 heavily pretreated patients, the ORR reached 83.3%, including a significant proportion achieving complete or VGPR. These outcomes align favorably with the MagnetisMM-3 trial, where an ORR of 61% was reported, increasing to over 70% in patients without prior BCMA therapy [2]. Similarly, in the MagnetisMM-1 phase 1 trial, elranatamab demonstrated an ORR of 73%, establishing early signals of robust efficacy [4]. Our study's median PFS of 8 months and median OS of 11 months, are comparable to those reported in published trial data. However, our analysis is limited by a small sample size and limited follow-up. Importantly, this reflects outcomes in a real-world population; many of whom would not

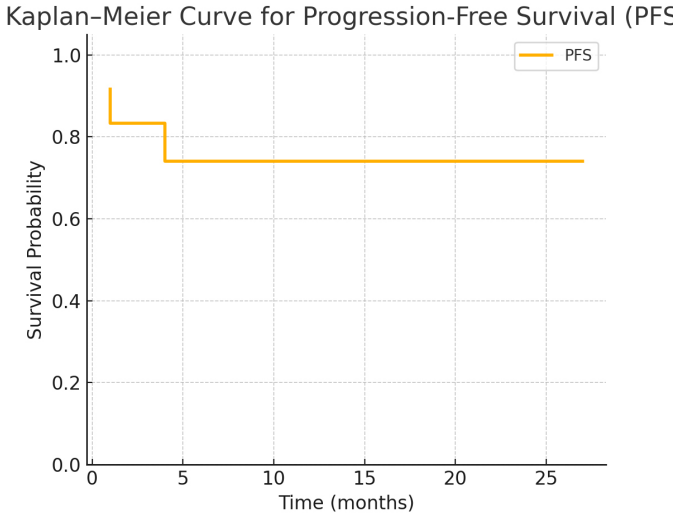

Figure 1. Kaplan-Meier estimate of progression-free survival

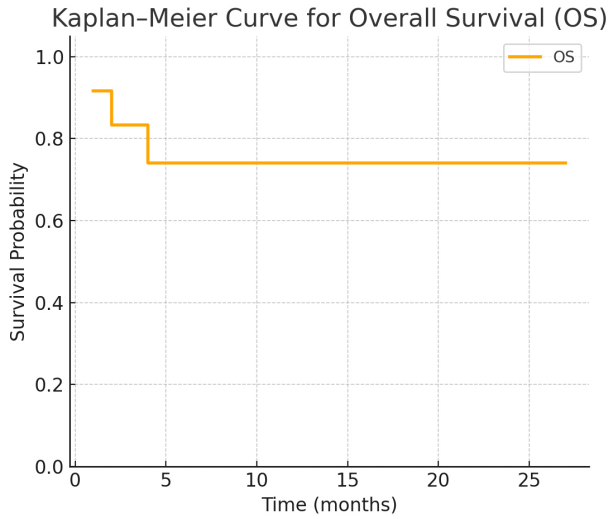

Figure 2. Kaplan-Meier estimate of overall survival

Table 1. Baseline characteristics of heavily pretreated myeloma patients treated with elranatamab

Characteristic	Value
Median age, years (range)	59.5 (39-73)
Gender, n (%)	Male: 7 (58.3%), female: 5 (41.7%)
MM type	IgG-kappa 5 (42%) IgA-kappa 4 (34%) IgG-lambda 1 (8%) IgA-lambda 1 (8%) Kappa monoclonal 1 (8%)
R-ISS-2 R-ISS-3	9 (75%) 3 (25%)
ECOG 1, n (%)	5 (42%)
ECOG 2, n (%)	2 (16%)
ECOG 3, n (%)	4 (34%)
ECOG 4, n (%)	1 (8%)
Standard risk cytogenetics, n (%)	9 (75%)
High risk cytogenetics, n (%)	3 (25%)
Median number of prior lines of therapy (range)	6.0 (4-8)
Presence of extramedullary disease, n (%)	Yes: 5 (41.7%), no: 7 (58.3%)
IgG level at treatment initiation (median, range) (mg/dL)	1261.5 (110-2900)
Received IVIG treatment, n (%)	Yes: 7 (58.3%), no: 5 (41.7%)

MM: Multiple myeloma, R-ISS: Revised international staging system, ECOG: Eastern Cooperative Oncology Group, IgG: Immunoglobulin G, IVIG: Intravenous immunoglobulin

qualify for trial enrollment due to comorbidities or frailty. Our findings also align with the results of the French Compassionate Use Program, highlighting similarly encouraging responses and underscoring the high rate of infectious complications, including CMV reactivation [5]. In our cohort, CMV reactivation occurred in 25% of patients, and grade 3 or higher infections were observed in 75%; necessitating stringent infection monitoring protocols. While CRS was common, it remained grade 1-2 and manageable in all cases. No ICANS events were observed. The administration of elranatamab in our center was logistically feasible, and treatment duration extended up to 27 cycles in some patients. This extended exposure suggests durable tolerability, in line with observations from the MagnetisMM-9 trial, which continues to evaluate long-term use and fixed-duration strategies [6].

Seval et al. [7] presented results from a single-center study comparing the efficacy of salvage autologous stem cell transplantation (ASCT), selinexor, and elranatamab in heavily pretreated myeloma patients. In this study, the patients who received elranatamab had significantly higher ORRs compared to salvage ASCT and selinexor (73% vs. 54% vs. 64.7%), and a longer 1-year PFS was reported (71.3% vs. 55.5% vs. 68.3%). Notably, patients receiving elranatamab had a higher rate of serious infections, compared to the other groups, and low-grade CRS, was reported in 69% of the patients. This data, along with the results from the MagnetisMM-17 trial [8], which included 20 relapsed and refractory MM patients, are both parallel to our study's results and reflect the efficacy of elranatamab, while highlighting the critical side effects associated with elranatamab treatment.

Study Limitations

This study has inherent limitations due to its retrospective design, small sample size, and brief follow-up period. However, its strengths lie in reflecting real-world practice, capturing toxicity profiles, and adding to the growing post-marketing evidence.

Conclusion

In this single-center retrospective analysis, elranatamab demonstrated high response rates and encouraging survival outcomes in a cohort of heavily pretreated, triple-class refractory MM patients. The treatment was generally well tolerated, though infectious complications, particularly CMV reactivation, were notable and underscore the need for proactive monitoring strategies. Our findings support the real-world effectiveness of elranatamab and provide additional clinical insight into its safety and feasibility outside of controlled trial settings. Larger prospective studies and extended follow-up are warranted to validate these outcomes and optimize supportive care strategies.

Ethic

Ethics Committee Approval: Approval was obtained from the Acıbadem University Ethics Committee for the study (decision no: 2025-08/64, date: 22.05.2025).

Informed Consent: Informed consent was obtained from all the patients for the use of medical data.

Footnotes

Financial Disclosure: The author declared that this study received no financial support.

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